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Applicant : Yoshinobu HANYU et al.

Group Art Unit: 1632

Serial No. : 09/810,483

Examiner: Arun Chakrabarti, Ph.D

Filed : March 19, 2001

For : POWDER CONTAINING PHYSIOLOGICALLY ACTIVE PEPTIDE

**AMENDMENT UNDER 37 C.F.R. § 1.111**

Commissioner of Patents and Trademarks  
Washington, D.C. 20231

Sir:

Responsive to the Final Office Action of January 15, 2002, reconsideration and withdrawal of the rejections made therein are respectfully requested, in view of the following amendments and remarks. Inasmuch as the three-month shortened statutory period was originally set in the Office Action to expire on April 15, 2002, Applicant hereby request an extension of time for two (2) months and are concurrently filing a formal Request for Extension of Time, together with all requisite fees therefor. If for any reason the formal Request for Extension of Time is not associated with the file at the Patent and Trademark Office or the extension fee is deficient, this should be considered to be an express request for any necessary extension of time and authorization for the Commissioner to charge any necessary extension of time fee to Deposit Account No. 19-0089.

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**IN THE CLAIMS**

Please amend claim 33 as follows:

33. (Amended) A powder containing a physiologically active peptide, wherein the powder comprises particles which particles comprise a physiologically active peptide and mannitol in a weight proportion of from 1:1 to 1:50, the particles further comprising per one part by weight of the physiologically active peptide at least one of a nonionic surfactant in an amount of 0.05-3 parts by weight, hydrogenated lecithin, and a binder selected from the group of polyvinylpyrrolidone, polyvinylalcohol, a water-soluble, nonionic, cellulose derivative, and mixtures thereof, in an amount of 0.05-6 parts by weight.

**REMARKS**

Reconsideration and withdrawal of the rejection in the outstanding Office Action are respectfully requested in view of the foregoing amendments and the following remarks.

***Preliminary Matters and Interview Summary***

Initially, Applicants thank the Examiner for granting an interview, conducted on May 23, 2002. Applicants note that the Interview Summary (Form PTO-413) indicates that a separate record of the substance of the interview is not necessary, however, for the record, Applicants express agreement with the Summary. During the interview, Applicants presented arguments as to why the documents of record are insufficient to establish a *prima facie* case of obviousness, and the Examiner disagreed therewith.

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Applicants also wish to thank the Examiner for withdrawing all §§ 112 and 102(b) and related 103(a) rejections.

Applicants note that the Examiner has not acknowledged receipt of the claim of priority and the priority documents in the Office Action. Applicant's respectfully request that the Examiner acknowledge receipt thereof and Applicants' claim of priority in the next communication from the Patent and Trademark Office.

Reconsideration and withdrawal of the rejections of record are respectfully requested.

***Summary of Status of Amendments and Office Action***

In the present amendment, claim 33 is amended. Therefore, claims 33-54 are pending in the application with claims 33-36 being independent. Applicants expressly reserve the right to pursue the non-elected invention in a divisional application.

In the Office Action, claims 33-54 are rejected under 35 U.S.C. § 103(a) over Maa et al. (U.S. Patent 6,284,282) in view of Knight et al. (U.S. Patent 6,017,549).

***Explanation and Support for Amendments***

Applicant submits that each of the foregoing amendments is fully supported by the specification. The Examiner's attention is also directed to pages 5-8, 18-19 and Figures 1-3, specifically, page 19 and Figure 3, showing the benefits on the stabilization of the peptide through use of hydrogenated lecithin.

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***Response to § 103(a) Rejection***

Claims 33-54 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Maa et al., (U.S. Patent No. 6,284,282) in view of Knight et al. (U.S. Patent No. 6,017,549). The Office Action asserts that Maa et al. teaches a powder made up of a physiologically active peptide and mannitol at a weight proportion of 1:1 to 1:50, the particles further comprising nonionic surfactant and a nonionic, water soluble binder (trehalose). The Office Action asserts that Maa et al. teaches the ratio of peptide and mannitol is precisely 1:1. The Office Action also asserts that Maa et al. teaches the drying a powder containing a physiologically active peptide by spray-freeze drying, the powder is used as an inhalant, the active peptide is hGH or insulin, and the particles sizes are 1-10  $\mu\text{m}$ . The Office Action asserts that the selection of the specific weight ratios of surfactant and binder represents routine optimization with regard to sequence, length and compositions, and that an ordinary practitioner explicitly recognizes such as routine optimization parameters in the relevant art. The Office Action asserts that Knight et al. teaches the use of hydrogenated lecithin as an ingredient, and it would have been obvious to one of ordinary skill in the art to combine and substitute the hydrogenated lecithin with the powder of Maa et al.

Initially, Applicants respectfully assert that the Office Action misapprehends the teachings of Maa et al. and the scope of the claims of Applicants invention. Applicants' claimed invention is to a powder containing a physiologically active peptide which comprises:

a physiologically active peptide

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+ mannitol in a weight proportion of from 1:1 to 1:50

+ per one part by weight of the physiologically active peptide at least one of a nonionic surfactant in an amount of 0.05-3 parts by weight

+ hydrogenated lecithin, and

+ a binder selected from the group of polyvinylpyrrolidone, polyvinylalcohol, a water-soluble, nonionic, cellulose derivative, and mixtures thereof, in an amount of 0.05-6 parts by weight.

By contrast, contrary to the assertions of the Office Action, Maa et al., at the places cited in the Office Action, teaches:

a peptide + mannitol (Table 3) = DNase/E25 + mannitol

a peptide + surfactant (Column 1) = rhGH + polysorbate-20 surfactant

a peptide + mannitol + a binder (Table 3) = E25 + trehalose.

In fact, Maa et al. does not teach or suggest the use of mannitol with a surfactant, much less mannitol plus a surfactant plus a peptide. Applicants, therefore, respectfully assert that Maa et al. does not teach or suggest the three (3) component system of claims 32-36 and 39-41, much less the four (4) component system of claims 33, 37, 41-54. Further, Maa et al. does not teach or suggest the weight ratios for the various components of the current inventions. The Office Action states that Knight et al. teaches only the use of hydrogenated lecithin to decrease irritation. Therefore, the cited combination does not teach or suggest Applicants invention.

Therefore, Applicants respectfully submit that the Office Action does not establish a *prima facie* case of obviousness as required by the law. Applicants note that when, as in the

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instant case, the claimed subject matter has been rejected as being obvious in view of a combination of prior art references, a proper analysis under 35 U.S.C. § 103 requires consideration of two factors: (1) whether the prior art would have suggested to one of ordinary skill in the relevant art at the time the invention was made that he should make the claimed product or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, one of ordinary skill in the art would have a reasonable expectation of success. In re Vaeck, 947 F.2d 488, 493 (Fed. Cir. 1991). "Both the suggestion and the expectation of success must be found in the prior art, not in the applicant's disclosure." In re Dow Chemical Co., 837 F.2d 469, 473 (Fed. Cir. 1988); see also Vaeck, 947 F.2d at 493.

As the Examiner is aware, in evaluating an alleged case of obviousness based upon a proposed combination of references, the "critical inquiry is whether 'there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination.'" In re Rouffet et al., No. 97-1492 (Fed. Cir. July 15, 1998); Fromson v. Advance Offset Plate, Inc., 755 F.2d 1549, 1556 (Fed. Cir. 1985)(Citing Lindemann Maschinenfabrik GmbH v. American Hoist and Derrick Co., 730 F.2d at 1462 (Fed. Cir. 1984), emphasis original). Whether the changes from the prior art required to establish a case of obviousness are minor or not, the question is "whether the prior art provides any teaching or suggestion to one of ordinary skill in the art to make the changes that would produce the patentee's method and device." Northern Telecom, Inc. v. Datapoint Corp., 908 F.2d 931, 935 (Fed. Cir. 1990).

"When prior art references require selective combination by the court to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight

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gleaned from the invention itself." In re Rouffet et al., No. 97-1492 (Fed. Cir. July 15, 1998); Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1143 (Fed. Cir. 1985).

"Virtually all inventions are combinations of old elements. Therefore an examiner may often find every element of a claimed invention in the prior art. If identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue. Furthermore, rejecting patents solely by finding prior art corollaries for the claimed elements would permit an examiner to use the claimed invention itself as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention. Such an approach would be an illogical and inappropriate process by which to determine patentability." In re Rouffet et al., 47 USPQ2d 1453, 1456 (Fed. Cir. 1998) (citations and quotation marks omitted).

To prevent the use of hindsight based on the invention to defeat patentability of the invention, the Federal Circuit requires the examiner to show a motivation to combine or modify the references that create the case of obviousness. In other words, the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed. In re Rouffet et al., 47 USPQ2d 1453, 1457 (Fed. Cir. July 15, 1998). See also In re Dance No. 48 USPQ2d 1635 (Fed. Cir. October, 1998).

The Federal Circuit has recently made clear that the foregoing analysis applies whether the argument is couched in terms of "combining teachings found in the prior art" or that the invention is an obvious modification of the prior art. Thus the "mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious

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unless the prior art suggested the desirability of the modification. Wilson and Hendrix [a combination of references proposed by the Examiner] fail to suggest any motivation for, or desirability of, the changes espoused by the Examiner and endorsed by the Board." In re Fritch, 972 F.2d 1260, 1266 (Fed. Cir. 1992).

Beyond the lack of any teaching or suggestion of a three component system in either Maa et al. or Knight et al. as discussed above, Applicants respectfully assert that the Office Action fails to point out any motivation to, or the desirability of combining Maa et al. with Knight et al. The Office Action's sole statement regarding motivation is that "Maa et al state, 'The present invention is directed to methods and compositions comprising spray freeze-dried formulations of therapeutic proteins, that show **good dispersibility and respirable properties**, as well as good stability'" and that "Knight et al further provides motivation as Knight et al state, 'In particular the invention relates to cosmetic and pharmaceutical **emulsions** which are **non irritating when applied to the skin.**" There is no motivation to combine a document which teaches a powder with "**good dispersibility and respirable properties**, as well as good stability" with a document teaching "**pharmaceutical emulsions** which are **non irritating when applied to the skin.**" Applicants respectfully assert that the Office Action has failed to point to any teaching within the cited documents which "provides any teaching or suggestion to one of ordinary skill in the art to make the changes that would produce the patentee's method and device." Northern Telecom, Inc. v. Datapoint Corp., 908 F.2d 931, 935 (Fed. Cir. 1990). Instead, the Office Action impermissibly employs "hindsight based on the invention to defeat patentability of the invention." In re Fritch.



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The Office Action states that the specific claimed weight ratios are "routine optimization parameters." However, for such a rejection, the particular parameter claimed must be recognized as a result-effective variable before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. In re Antoine, 559 F.2d 618, 620, 195 U.S.P.O. 6 (C.C.P.A. 1977). A result-effective variable is a variable whose modification achieves a recognized result. *Id.* at 620. The claims must be based upon optimum or workable conditions. *Id.* Here, Applicants' claims recite combination of components at certain weight ratios. As the Office Action has failed to show that the combination of components is obvious or known, *a fortiori*, the specific weight ratios of a non-obvious composition cannot render the composition obvious. Therefore, Applicants respectfully submit that the rejection is untenable and should be withdrawn.

In view of the above, Applicants respectfully request that this ground of rejection be withdrawn.

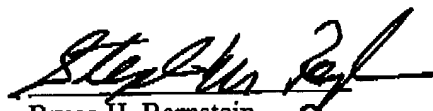
### ***Conclusion***

For the foregoing reasons, it is believed that all of the claims in this application are in condition for allowance, which action is respectfully requested. Applicants have addressed the Examiner's art based rejection and pointed to the fallacies contained within them, as discussed above. Thus it is believed that all of the claims are in condition for allowance, which action is respectfully requested.

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If the Examiner has any questions, or wishes to discuss this matter, the Examiner is respectfully invited to contact the undersigned at the below-listed telephone number.

Respectfully submitted,  
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